USARIEM TECHNICAL REPORT

T00-19

EFFECT OF SMOKING ON CUTANEOUS VASCULAR RESPONSES TO EXERCISE IN HEALTHY, EXERCISE-TRAINED, HEAT-ACCLIMATED HUMANS

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May, 2000

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REPORT DOCUMENTATION PAGE

Form Approved
OMB No. 0704-0188

1. AGENCY USE ONLY *(Leave blank)*	2. REPORT DATE	3. REPORT TYPE AND DATES COVERED
	May 2000	Technical Report

4. TITLE AND SUBTITLE
Effect of Smoking on Cutaneous Vascular Responses to Exercise in Healthy, Exercise-Trained, Heat-Acclimated Humans

5. FUNDING NUMBERS

6. AUTHOR(S)
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7. PERFORMING ORGANIZATION NAME(S) AND ADDRESS(ES)
U.S. Army Research Institute of Environmental Medicine
Natick, MA 01760-5007

8. PERFORMING ORGANIZATION REPORT NUMBER

9. SPONSORING / MONITORING AGENCY NAME(S) AND ADDRESS(ES)

10. SPONSORING / MONITORING AGENCY REPORT NUMBER

11. SUPPLEMENTARY NOTES

12a. DISTRIBUTION / AVAILABILITY STATEMENT

Approved for public release: Distribution unlimited.

12b. DISTRIBUTION CODE

13. ABSTRACT *(Maximum 200 words)*
The purpose of this study was to examine vascular responses to exercise in individuals with a risk factor for atherogenesis compared to individuals who did not share that particular risk. It was hypothesized that smokers (S; n=4) had less compliant cutaneous vessels than nonsmokers (NS; n=4). Esophageal (Tes) and skin temperatures (Tsk), heart rate (HR), blood pressure, forearm skin blood flow (SkBF) and forearm blood flow (FBF) were measured at rest, during 30 min cycle exercise (60% peak aerobic power), following arterial occlusion (reactive hyperemia) and during recovery at 30°C. Tes, Tsk and FBF were not different between S and NS at rest, during exercise or recovery. HR was higher in smokers at rest (S=69+9; NS=58+5 bpm; p=0.05) and during recovery (S=90+10; NS=75+10 bpm; p=0.07), but not different during exercise. During hyperemia, cutaneous vascular conductance (SkBF/MAP) averaged 3.5 ml/100ml/min/Torr lower in S than NS (p=0.03). Thermoregulatory responses were not compromised during the 30-min exercise in a warm environment. However, during recovery, HR was increased and reactive hyperemia was decreased in smokers. These data suggest reduced vascular compliance in the smokers, which might affect skin vascular responses during longer duration work or work done in a warmer environment.

14. SUBJECT TERMS
Core temperature, smoking, reactive hyperemia, skin temperature, skin blood flow, blood pressure

15. NUMBER OF PAGES

16. PRICE CODE

17. SECURITY CLASSIFICATION OF REPORT	18. SECURITY CLASSIFICATION OF THIS PAGE	19. SECURITY CLASSIFICATION OF ABSTRACT	20. LIMITATION OF ABSTRACT
Unclassified	Unclassified	Unclassified	

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ACKNOWLEDGEMENTS

We thank the volunteers for participating in the study and the physicians who provided medical monitoring for the study, including Drs. Jonathan Cañete, Verne Backus and COL Kevin Keenan. We thank Mr. Scott Robinson for preparing the graphics and formatting the document.

EXECUTIVE SUMMARY

This purpose of this research was to determine whether healthy, exercise-trained, heat-acclimated people with one major risk factor for coronary artery disease (smoking) would have a different cutaneous vascular response to exercise in a warm environment compared to people who were of similar age, gender, physical fitness, and heat acclimation state and who had similar total cholesterol/high density lipoprotein cholesterol. In the current study, we examined the cutaneous vascular responses of healthy smokers for signs of impairment in the peripheral vasculature that could be detected noninvasively prior to any evidence of coronary or aortic pathology. It was hypothesized that smokers (n=4) had less compliant cutaneous vessels than nonsmokers (n=4). Esophageal (T_{es}) and skin temperatures (T_{sk}), heart rate (HR), blood pressure, forearm skin blood flow (SkBF) and forearm blood flow (FBF) were measured at rest, during 30 min cycle exercise (60% peak aerobic power), following arterial occlusion (reactive hyperemia) and during recovery at 30°C. T_{es}, T_{sk} and FBF were not different between smokers and nonsmokers at rest, during exercise or recovery. HR was higher in smokers at rest (S=69±9; NS=58±5 bpm; p=0.05) and during recovery (S=90±10; NS=75±10 bpm; p=0.07), but not different during exercise. During hyperemia, cutaneous vascular conductance (SkBF/MAP) averaged 3.5 ml/100ml/min/Torr lower in S than NS (p=0.03). Thermoregulatory responses were not compromised during the 30-min exercise in a warm environment. However, during recovery, HR was increased and reactive hyperemia was decreased in smokers. These data suggest reduced vascular compliance in the smokers, which might affect skin vascular responses during longer duration work or work done in a warmer environment. The findings in this study, although limited for broad interpretation by subject number, further underscore the damage cigarette smoking does to the health of young soldiers. Further research is warranted to determine whether some of the procedures used in the current study could be used to assess degree of cardiovascular impairment in a larger population of healthy smokers.

INTRODUCTION

Scientific Background

Major risk factors for coronary artery disease include smoking, high total cholesterol/ high-density lipoprotein cholesterol or other dyslipidemias, hypertension, diabetes, physical inactivity and obesity (Rippe, J. M. & O'Brien, D., 1999). Previous studies have documented impaired forearm skin blood flow in smokers (Celermajer, D. S. et al., 1992), hypercholesterolemic individuals (Casino, P. R., Kilcoyne, C. M., Quyyumi, A. A., Hoeg, J. M., & Panza, J. A., 1993; Celermajer, D. S. et al., 1992; Chowienczyk, P. J., Watts, G. F., Cockcroft, J. R., & Ritter, J. M., 1992; Drexler, H., Zeiher, A. M., Meinzer, K., & Just, H., 1991), hypertensive men (Calver, A., Collier, A. J., Moncada, S., & Vallance, P., 1992), and diabetic men (Fortney, S. M, Koivisto, V. A., Felig, P., & Nadel, E. R., 1981; Pieper, G. M., Gross, G. J., & Inc., 1991) compared to normal controls. In all the major risk categories for coronary artery disease listed above, endothelial dysfunction has been indicated (Luscher, T. F., Tanner, F. C., Tschudi, M. R., & Noll, G., 1993).

Although major risk factors for coronary artery disease were defined epidemiologically by coronary artery pathology, endothelial dysfunction may not be confined to the coronary arteries. It was hypothesized that relatively young individuals who smoked, would have similar deleterious effects on the cutaneous vasculature as documented by pathological studies for the coronary arteries and aorta (Anonymous 1990; Strong, J. P. et al., 1999). That is, individuals who smoke would have less compliant cutaneous vessels than individuals who did not smoke. The hypothesized relative endothelial dysfunction in the cutaneous arterial bed in individuals who smoke may contribute to impaired sensible heat dissipation as sensible heat flux is dependent upon vasomotor regulation of the cutaneous vasculature.

In the current study, we examined the cutaneous vascular responses for signs of impairment in the peripheral vasculature that could be detected noninvasively prior to any evidence of coronary or aortic pathology. Obtaining evidence for impaired heat dissipation was limited by the study design because the volunteers were studied in a

moderately hot environment with a moderate humidity. This conservative approach was used because there was a primary risk factor for coronary artery disease. Recently (Strong, J. P. et al., 1999) it was concluded that atherosclerosis begins in youth (15- to 34-year age span). Fatty streaks and raised lesions were observed in the aortas and frequently in the right coronary arteries upon autopsy in young people who died from external causes. The degree of pathology has been related to smoking in this young population (Anonymous, 1990).

Purpose

The purpose of this research study was to examine vascular responses to exercise in individuals with a risk factor for coronary artery disease compared to individuals who did not share that particular risk. It was hypothesized that individuals who smoked, would have less compliant cutaneous vessels than individuals who did not smoke. In effect, we studied the cutaneous vascular responses during an exercise task in a specific group of individuals with a primary risk factor to determine whether or not noninvasive measurement of peripheral vascular responses shows functional impairment prior to any known evidence of coronary or aortic pathology. Individuals in this risk group may have impaired sensible heat dissipation as sensible heat flux is dependent upon vasomotor regulation of the cutaneous vasculature. As a safety precaution, the volunteers were studied in a moderately hot environment with a moderate humidity even though impaired heat dissipation was hypothesized for the smokers. This safety precaution had the effect of minimizing our ability to resolve differences between the risk factor group and the control group.

Military Relevance

Twenty-five percent of the population studied in the U.S. Army Health Promotion Program which includes active-duty Army, Army National Guard, U.S. Army reserve and civilians working in the Department of the Army smoke (Rao, V., 1999). Young men, lower rank Enlisted and personnel other than active-duty Army were less likely to meet the Health Promotion Program standards. Descriptions of vascular pathology in young people who smoke (Strong, J. P. et al., 1999) raised the question of whether a subset of the population of active-duty soldiers (age range 19-42 years) are at greater propensity for heat illness or injury due to functional impairment of the cutaneous vasculature. If

this is the case, there might be an even greater incidence of heat injury or incidence of coronary artery disease in the Army Reserve and National Guard as the prevalence of smoking is greater in these groups compared to active-duty Army personnel (Rao, V., 1999).

Vascular evidence of coronary artery disease or atherosclerosis is usually not obtained in healthy young people. The current research was done to test for symptoms of functional impairment in vasomotor regulation in healthy people by observing the responses of the cutaneous vasculature to exercise. Individuals who smoke may exhibit some functional impairment in the cutaneous vasculature during exercise that is associated with increased arterial resistance during exercise. If functional impairment of the cutaneous vasculature occurs during exercise, it might be expected that these individuals have a greater propensity for heat illness or heat injury.

METHODS

Test Subjects

Eight people (6 men and 2 women) volunteered to do the study after they were formally briefed on the design and risks of the study. All volunteers exercised habitually and were acclimated to heat. Table 1 shows the subject characteristics. Female volunteers were studied in the early follicular phase of the menstrual cycle. None of the volunteers were medicated and use of aspirin and ibuprofen was prohibited for 10 days prior to an experiment. Volunteers learned the procedures used in the experiments and

Table 1

Gender	TC/HDL-C	Age (yr)	Height (cm)	Weight (kg)	Peak Aerobic Power (L/min)	(ml/min/kg)
Nonsmokers						
Male	3.45	40	177.8	81.8	3.358	41.05
Male	3.04	22	185	78.1	4.195	53.71
Female	4.18	46	157.5	58.2	1.780	30.58
Male	5.42	28	190.5	88.6	4.566	51.54
Mean	**4.03**	**34**	**177.7**	**76.7**	**3.475**	**44.22**
S.D	(1.04)	(11)	(14.4)	(13.1)	(1.238)	(10.64)
Smokers						
Male	3.51	32	170.2	73	3.387	46.40
Male	3.32	19	175	73.4	3.840	52.32
Female	4.21	34	157.5	59.1	1.979	33.49
Male	4.73	24	173	89.5	3.682	41.14
Mean	**3.94**	**27.3**	**168.9**	**73.75**	**3.222**	**43.34**
S.D.	(0.65)	(6.99)	(7.87)	(12.48)	(0.850)	(8.00)
P	ns	ns	ns	ns	ns	ns

were also familiarized with the investigators by attending up to five procedural training sessions.

Environmental Conditions

The ambient dry bulb temperature was 30°C and the ambient dew-point temperature was 12°C.

Experimental Design

Each volunteer did an exercise experiment on each of three separate days with at least one day between experiments.

Test Procedures

The test subjects fasted overnight, and refrained from drinking alcohol 24 h prior to the experiment. Water ingestion was permitted until the experiment started. Smokers refrained from smoking upon awakening and prior to the experiments. Before the experiment, a 5- ml venous blood sample was drawn for determination of triglycerides, total cholesterol and HDL cholesterol (Sigma). Laboratory accreditation for the cholesterol assay was obtained through Northwest Lipids. The time of the experiment was approximately the same time of day for each test subject for all experiments (starting between 0700-0730 h) to control for circadian differences in skin blood flow and thermoregulation.

Exercise Test

The test subjects entered the environmental test chamber dressed in shorts, singlet, shoes, socks and underwear. Male subjects often chose not to wear the singlet, but the clothing chosen was the same for all experiments. Electrocardiographic electrodes and leads were attached to the torso. A thermistor or thermocouple encapsulated in water-proof insulation was swallowed by the subject for the measurement of esophageal temperature (T_{es}). The esophageal thermocouple was inserted to a depth of about 25% of the individual's height. The volunteer was weighed and then sat on the chair of the modified cycle ergometer. Thermocouples (copper-constantan) were attached to the skin at eight sites. Venous occlusion plethysmography (Hokansen, Bellevue, WA) was used to measure forearm blood flow (FBF) (Doherty, T. J., Stephenson, L. A., Kolka, M. A.,

Sexton, G. N., & Gonzalez, R. R., 1993; Whitney, R. J., 1953) and laser doppler velocimetry (Vasamedics, St. Paul, MN) was used to measure skin blood flow (SkBF) (Johnson, J. M., Taylor, W. F., Shepherd, A. P., & Park, M. K., 1984) on the forearm and chest. Local skin sweating rate was measured on the forearm in a contralateral position to the laser doppler probe. An automatic blood pressure monitor (Datascope, Inc., Paramus NJ) was used to determine systolic and diastolic blood pressure.

Figure 1

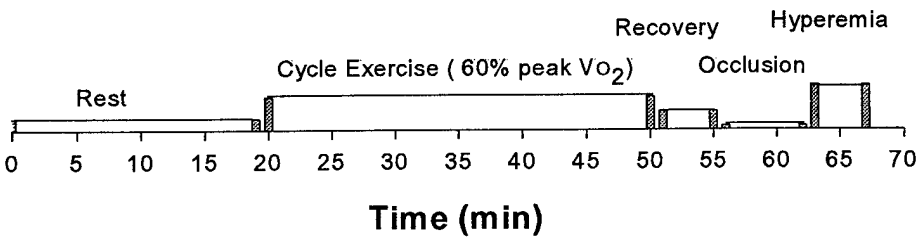


Figure 1 is a timeline showing the sequence of events for each experiment. After all instruments were attached to the subject, a 20-min control period was started. Esophageal and skin temperatures, forearm blood flow, skin blood flow, and local sweating rate were measured every 0.5 min, and blood pressure and heart rate were measured every 5 min. The subject exercised for 30 min at 60% peak VO_2 during which time the temperature, blood flow and heart rate measurements were made at the same time intervals as during rest. Blood pressure was measured every 2.5 min. Exercise ended after 30 min and the volunteer recovered for five minutes. Arterial occlusion was then initiated. Occlusion lasted 7 min except for two subjects who could tolerate only 5 min (S2 and S3). After occlusive pressure was released, skin blood flow was measured to gauge the hyperemic response. After the experiment, the subject was weighed.

Data Analyses.

The results for the three exercise tests were averaged to give a mean response for each physiologic measure in each subject. Physiologic responses were analyzed by two-

way analysis of variance (Group X Time) between smokers and the nonsmokers. When there was a significant interaction between group and time, the data set was segmented into rest, exercise, and recovery periods.

T tests were done to compare data between groups when time was not an included factor. Specifically, unpaired T tests were done to compare subject characteristics. Unpaired T tests were done to compare change in esophageal temperature at the initiation of exercise, duration of change in esophageal temperature at the initiation of exercise, and cutaneous vascular conductance during the hyperemic response. Significant differences was accepted as $\alpha = 0.10$.

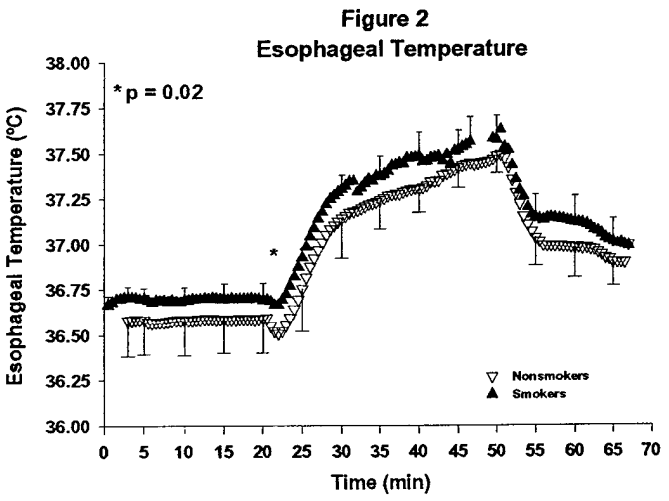
Given the small number of subjects in each group, $\alpha = 0.10$ was chosen. Thus, a probability of less than 10% was judged to be a significant difference between groups. By choosing this probability level, a Type I error may be made such that the null hypothesis is rejected when it, in fact, is true in 10% of the cases. This α-level was more comfortably chosen because each subject did the exercise test three times. These data were averaged to reduce the error variance for each subject and used in the statistical analyses. By using the mean data, the possibility of a Type II error was reduced.

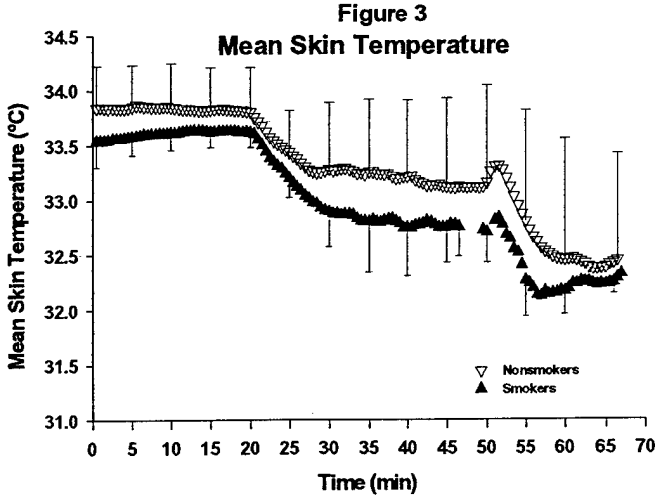
RESULTS AND DISCUSSION

Thermal Responses

There were no significant differences between smokers and non-smokers for esophageal temperature (p=0.192, Figure 2) or mean skin temperature (P=0.41, Figure 3). However, during recovery from exercise there was a significant interaction between group and time (p=0.10) in mean skin temperature.

There is a characteristic decrease in esophageal temperature in nonsmokers. This characteristic has been interpreted as cooling of the body core after cooler blood from the skin (body shell) is shunted internally by vasoconstriction in response to release of catecholamines at the beginning of exercise (Johnson, J. M. & Park, M. K., 1982). In smokers, the esophageal temperature reduction at the initiation of exercise was blunted





compared to nonsmokers (Figure 2). The change in esophageal temperature at the beginning of exercise was less (0.05°C, P=0.02) and its duration was shorter (1 min, P=0.05) in smokers. These observations suggest that the exercise-induced vasoconstriction was modulated in smokers. Although T_{sk} was not different between smokers and nonsmokers in this study which was conducted in a warm environment, in general smokers have cooler skin than do nonsmokers (Goldsmith, J. R. & Landaw, S. A., 1968). Cooler skin may indicate that the cutaneous vasculature of smokers is normally relatively constricted compared to nonsmokers. Cutaneous skin blood flow of smokers may already be constricted to the extent that initiation of exercise causes little additional

vasoconstriction. This might explain why there is only a slight decrease in esophageal temperature at the onset of exercise in smokers.

Forearm blood flow appeared to be higher in smokers (p=0.11, Figure 4). Sweating was not different between the smokers and the nonsmokers (Figure 5). Forearm skin blood flow as measured by laser Doppler was not different between smokers and nonsmokers. The apparent increase in FBF in the smokers compared to non-smokers with no apparent difference in skin blood flow indicates the increase blood flow must be in the skeletal muscle compartment. Increased forearm skeletal muscle blood flow might be due to activation of nicotinic receptors in the muscle vasculature so that muscle is perfused preferentially. Despite the fact that nicotine causes cutaneous vasoconstriction (Jaffe, J. H., 1991), nicotine should have been cleared from the plasma because the smokers in the current study had refrained from smoking upon awakening until the experiments were completed. It has been reported recently that carboxyhemoglobin (18%) increases muscle blood flow in exercising humans (Gonzalez-Alonso, J., Richardson, R. S., & Saltin, B., 2000). Smokers have a median carboxyhemoglobin level of about 6% (Goldsmith, J. R. & Landaw, S. A., 1968). It may be that muscle blood flow is modulated by mechanisms activated by nicotine and/or carbon monoxide binding for a net increase in muscle blood flow in smokers. If there is a greater distribution of cardiac output to the muscle in smokers, there may be less available to the skin thereby contributing to the reduced cutaneous vasoconstrictor activity in smokers at the beginning of exercise.

Figure 4
Forearm Blood Flow

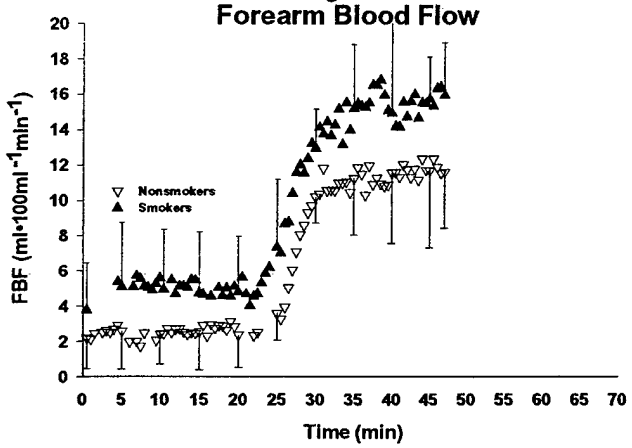
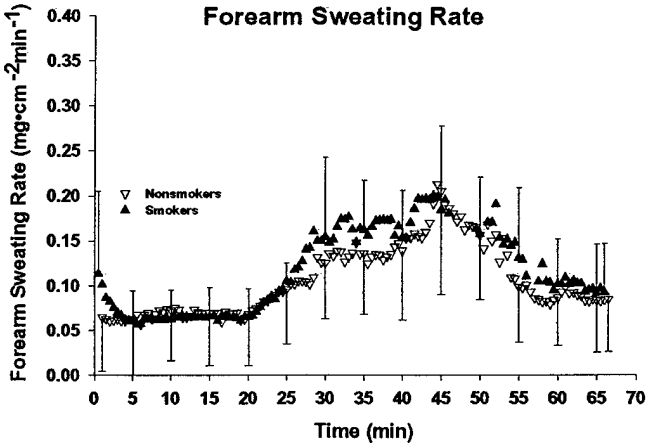


Figure 5
Forearm Sweating Rate



Cardiovascular Responses

In comparing smokers and nonsmokers, diastolic blood pressure was not different during the experiment (Figure 6). Heart rate was increased in smokers (p=0.06, Figure 7). There was a significant time by group interaction (p=0.03), so the heart rate data was divided into rest, exercise and recovery data sets. In smokers, heart rate was elevated during rest (p=0.052) and recovery (p=0.077), but not different during exercise (Figure 7).

The exercise intensity was set to 60% of peak aerobic power, so that explains why there were no differences between the smokers and non-smokers during exercise. It is known that smoking affects the coronary vasculature, so the elevated resting heart rate in the smokers is expected. The smokers' heart rate was elevated during recovery

Figure 6
Diastolic Pressure

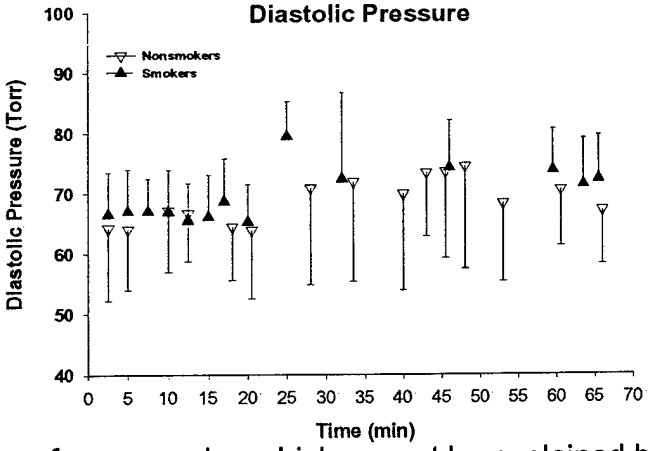
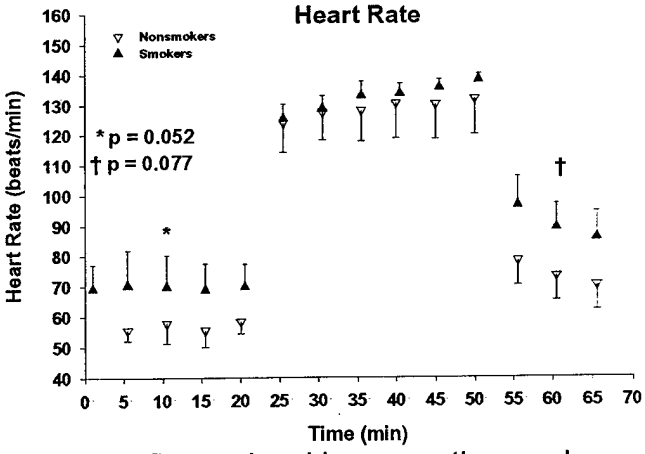


Figure 7
Heart Rate



from exercise which cannot be explained by physical fitness level because the smokers had a similar aerobic power as the non-smokers (Table 1). On the other hand, smokers are known to have elevated levels of carbon monoxide which binds to hemoglobin so oxygen-binding capacity would be detrimentally affected (Goldsmith, J. R. & Landaw, S. A., 1968). Additionally, pathologic coronary vessels have been described in young smokers (Anonymous, 1990). These facts taken together might explain why coronary recovery as measured by heart rate was affected in the smokers.

Cutaneous vascular conductance (CVC) was not different between the two groups. There was no difference in FVC between smokers and non-smokers (Fig. 9, p=0.156). Only during the reactive hyperemia test was CVC less in smokers than non-smokers (Fig. 8, p=0.03).

Figure 8
Cutaneous Vascular Conductance

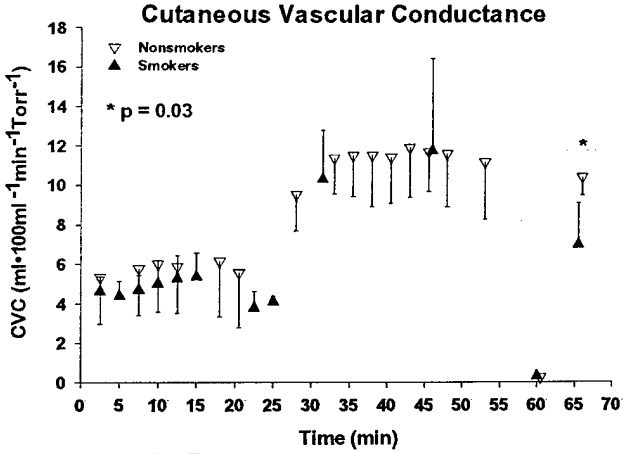
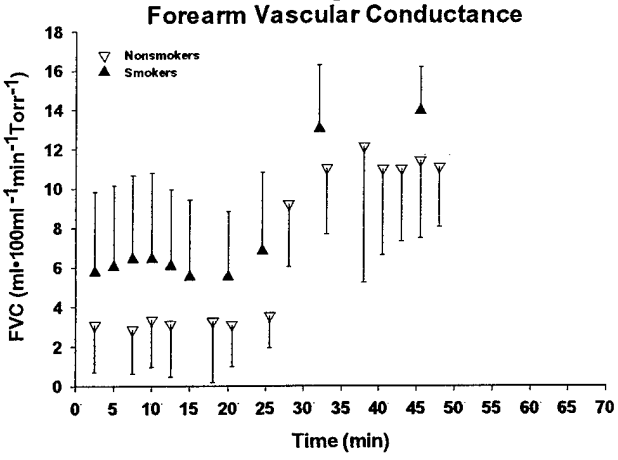


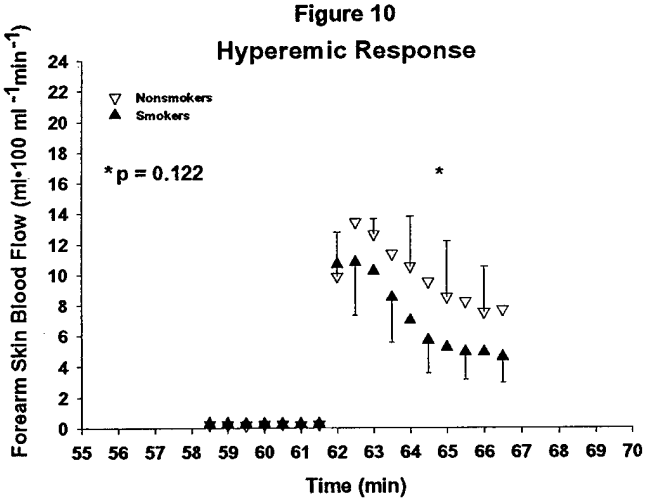
Figure 9
Forearm Vascular Conductance



Hyperemic Responses

Figure 10 shows the reactive hyperemic response to arterial occlusion done between minutes 55-62 of the experiment. The smokers did not attain the magnitude of hyperemia that the nonsmokers did (Figure 10, p=0.122). The observation that mean skin temperature of smokers recovered in a different pattern than non-smokers (Figure 3) implies that pooled blood in a compartment other than the skin (because skin blood flow was lower in the smokers) is responsible for the increase in skin temperature. Note also that the mean skin temperature of the smokers is still less than the nonsmokers which is consistent with the decreased magnitude of reactive hyperemia in the smokers. That is, the blood flow to the surface of the skin is reduced. It may be that forearm muscle blood flow is increased in the smokers thereby reducing the fraction of cardiac output available to the skin as shown by the reduced CVC in smokers during the hyperemic response (Fig 8). This explanation is in line with the earlier observation that forearm muscle blood flow is increased in smokers (Fig 4, P=0.11).

Figure 10
Hyperemic Response



CONCLUSIONS

Subjects in both groups routinely exercised and were heat-acclimated. The smokers' thermoregulatory responses were not compromised during the moderately heavy exercise done for 30 min in a warm environment, although smokers do have a reduced vasoconstrictor response at the initiation of exercise compared to non-smokers. The smokers' increased heart rate during recovery from exercise and the decrease reactive hyperemia as measured by skin blood flow and cutaneous vascular conductance suggests compromised coronary recovery and reduced vascular compliance in the smokers. These differences in smokers might affect the thermoregulatory responses of smokers during longer duration work and work done in a hot environment.

The experimental procedures used in this research protocol might be one noninvasive method to test for compromised arterial resistance or vascular compliance in healthy, physically-fit people, and should be validated in a larger population. In particular, occlusion of the brachial artery and subsequent measurement of the magnitude of reactive hyperemia may be a very useful screening tool for assessing degree of vasomotor impairment in the cutaneous vasculature of smokers or others with a high risk for coronary artery disease. The damage cigarette smoking does to the health of young soldiers is underscored by the findings in this study, despite the small subject number. When the impact that smoking has on cardiovascular responses to exercise and arterial occlusion is added to other detrimental effects of smoking on young soldiers including increased incidence of exercise-related injuries in young soldiers in Army basic training (Altarac, M. et al., 2000), bone fracture (Friedl, K. E. & Nuovoa, J. A., 1992; Reynolds, K. L. et al., 1994) and healing (Haverstock, B. D. & Mandracchia, V. J., 1998) and reduced tissue healing (Davies, B. W., Lewis, R. D., & Pennington, G., 1998; Jorgensen, L. N., Kallehave, F., Christensen, E., Siana, J. E., & Gottrup, F., 1998), the necessity for the U.S. Army Health Promotion Program is further underscored.

RECOMMENDATIONS

It is suggested that assessment of the reactive hyperemic response to brachial artery occlusion when done in a warm environment may be developed as a method to show compromised vasomotor regulation in the cutaneous vasculature. Further extensive research would be required to develop standards to identify compromised vasomotor regulation. The benefit from such an endeavor would be to individually demonstrate the detrimental effects that smoking inflicts on relatively young, physically-fit and heat-acclimated people.

REFERENCES

Anonymous. Relationship of atherosclerosis in young men to serum lipoprotein cholesterol concentrations and smoking. A preliminary report from the pathobiological determinants of atherosclerosis in youth (PDAY) research group. (1990). Journal of the American Medical Association 264:3018-3024.

Altarac M, Gardner JW, Popovich RM, Potter R, Knapik JJ, Jones BH (2000). Cigarette smoking and exercise-related injuries among young men and women. American Journal of Preventive Medicine 18:96-102.

Calver A, Collier AJ, Moncada S, Vallance P (1992) Effect of local intra-arterial NG-monomethyl-L-arginine in patients with hypertension: the nitric oxide dilator mechanism appears abnormal. Journal of Hypertension 10:1025-1031.

Casino PR, Kilcoyne CM, Quyyumi, AA, Hoeg JM, Panza JA (1993) The role of nitric oxide in endothelium-dependent vasodilation of hypercholesterolemic patients. Circulation 88:2541-2547.

Celermajer DS, Sorensen KE, Gooch VM, Spiegelhalter, SJ, Miller OI, Sullivan ID, Lloyd JK, Deanfield JE (1992). Non-invasive detection of endothelial dysfunction in children and adults at risk of atherosclerosis. Lancet 340:1111-1115.

Chowienczyk PJ, Watts GF, Cockcroft, JR, Ritter JM (1992). Impaired endothelium-dependent vasodilation of forearm resistance vessels in hypercholesterolemia. Lancet 340:1430-1432.

Davies BW, Lewis RD, Pennington G (1998). The impact of vasodilators on random-pattern skin flap survival in the rat following mainstream smoke exposure. Annals of Plastic Surgery 40:630-636.

Doherty TJ, Stephenson LA, Kolka, MA, Sexton GN, Gonzalez, RR (1993). Automated strain gauge plethysmograph. U.S.Army Research Institute of Environmental Medicine Technical Report T??-?? Natick, MA 01760-5007.

Drexler H, Zeiher AM, Meinzer K, Just H (1991). Correction of endothelial dysfunction in coronary microcirculation of hypercholesterolaemic patients by L-arginine. Lancet 338:1546-1550.

Fortney SM, Koivisto VA, Felig P, Nadel ER (1981). Circulatory and temperature regulatory responses to exercise in a warm environment in insulin-dependent diabetics. Yale Journal of Biology and Medicine 54:101-109.

Friedl KE, Nuovoa JA (1992). Factors associated with stress fracture in young Army women: Indications for further research. Military Medicine 157:334-338.

Goldsmith JR, Landaw SA (1968). Carbon monoxide and human health. Science 162:1352-1359.

Gonzalez-Alonso J, Richardson RS, Saltin B (2000). Effect of carbon monoxide on muscle blood flow and oxygen uptake during submaximal exercise in humans. FASEB Journal 14: A669.

Haverstock BD, Mandracchia VJ (1998). Cigarette smoking and bone healing: implication in foot and ankle surgery. Journal of Foot and Ankle Surgery 37: 69-74.

Jaffe, J. H. (1991). Drug addiction and drug abuse. In A.G.Gilman, T. W. Rall, A. S. Nies, & P. Taylor (Eds.), Goodman and Gilman's The Pharmacological Basis of Therapeutics (8th ed., pp. 522-573). New York: Pergamon Press.

Johnson JM & Park, MK (1982). Effect of heat stress on cutaneous vascular responses to the initiation of exercise. Journal of Applied Physiology 53:744-749.

Johnson JM, Taylor WF, Shepherd AP, & Park MK (1984). Laser-Doppler measurement of skin blood flow: comparison with plethysmography. Journal of Applied Physiology 56:798-803.

Jorgensen LN, Kallehave F, Christensen E, Siana JE, Gottrup F (1998). Less collagen production in smokers. Surgery 123:450-455.

Lüscher TF, Tanner FC, Tschudi MR, Noll G (1993). Endothelial dysfunction in coronary artery disease. Annual Review of Medicine 44:395-418.

Pieper GM, Gross GJ (1991). Endothelial dysfunction in diabetes. Cardiovascular Significance of Endothelium-Derived Vasoactive Factors pp. 223-262.

Rao V (1999). Quantitative analysis of the U.S. Army Health Promotion Program Health Risk Appraisal Database. Summary Report: 1991-1995 U.S. Army Center for Health Promotion and Preventive Medicine Summary Report Aberdeen Proving Ground, MD

Reynolds KL, Heckel HA, Witt CE, Martin JW, Pollard JA, Knapik JJ, Jones BH (1994). Cigarette smoking, physical fitness, and injuries in infantry soldiers. American Journal of Preventive Medicine 10:145-150.

Rippe JM and O'Brien D (1999). The rationale for intervention to reduce the risk of coronary artery disease. In J.M.Rippe (Ed.), Lifestyle Medicine, pp. 40-53. Malden, MA: Blackwell Science, Inc.

Strong JP, Malcom GT, McMahan CA, Tracy, RE, Newman WPIII, Herderick JF, Cornhill JF (1999). Prevalence and extent of atherosclerosis in adolescents and young adults. Implications for prevention from the pathobiologic determinants of atherosclerosis in youth study. Journal of American Medical Association 281:727-735.

Whitney RJ (1953). The measurement of volume changes in human limbs. Journal of Physiology (London) 121:1-27.